How standards are *accelerating* the adoption of machine source radiation sterilization

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Identifying the need

- For the medical device industry to continue to grow, we need to provide more options for radiation sterilization
- In order to take advantage of machine source radiation, guidance can help organizations understand fundamentals of:
  - Designing products for radiation
  - Transferring products from one radiation source to another
- The collaboration between industry and regulatory and between standards organizations is helping to fill this gap

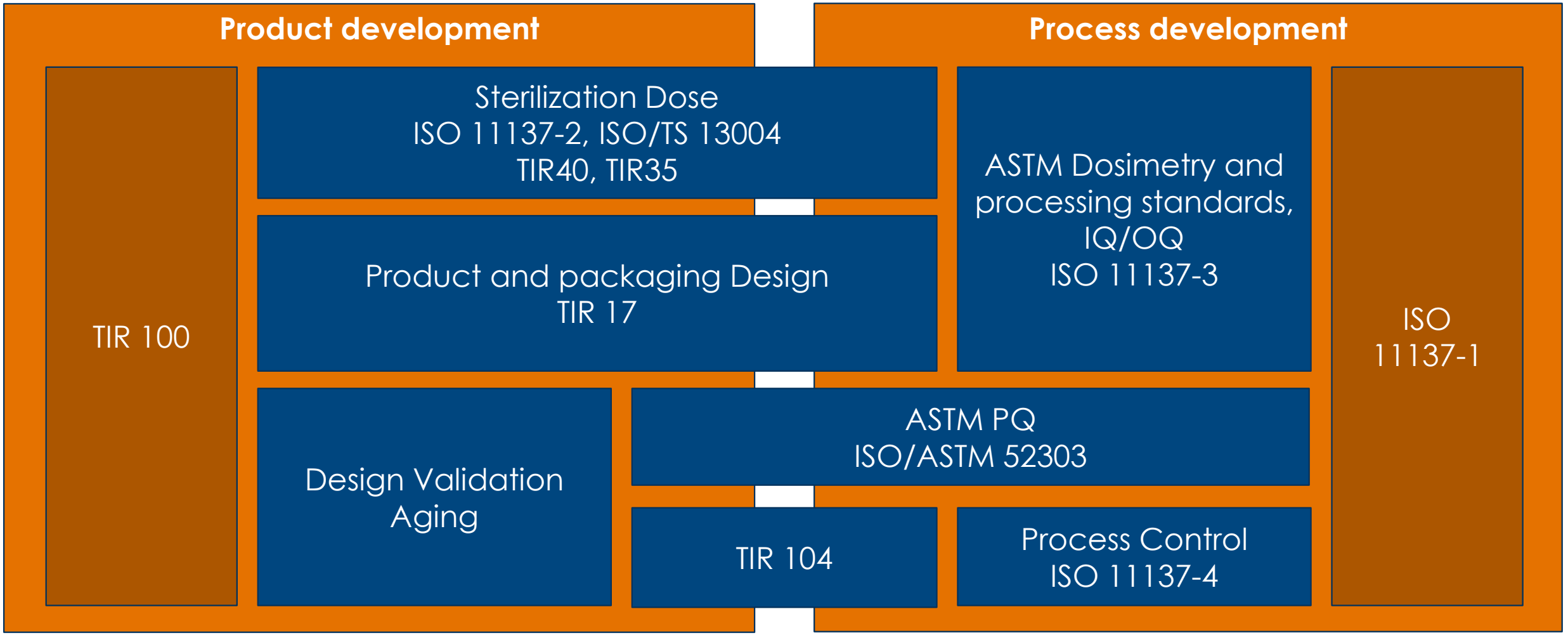
Relevant Standards Organizations

- AAMI ST – Sterilization Standards Committee
  - WG2 Radiation Sterilization
  - WG8 Microbiological Methods
  - WG15 Assurance of Sterility
  - WG96 Compatibility of Materials
- ASTM E61 Radiation Processing
  - E61.01 Dosimetry
  - E61.02 Dosimetry Systems
  - E61.03 Dosimetry Applications
  - E61.04 Specialty Applications
- ISO TC198 Sterilization of health care products

How standards help

- Recent work in standards is helping to lay the groundwork for easing the transfer between sterilization modalities
  - Ready for publication: **TIR100**, ***End-to-end microbiological quality and sterility assurance***
  - Ballot passed, preparing final draft for review: **TIR104**, ***Guidance on transferring health care products between radiation sterilization sources***
  - Work started on revision to **ISO 11137-1**, ***Requirements for development, validation and routine control of a sterilization process for medical devices***
  - New revision initiated: **TIR17**, ***Compatibility of materials subject to sterilization***
  - New ASTM standards on modality specific OQ

How standards for radiation sterilization work



TIR100 – End-to-end

- What is meant by end-to-end?

- Decisions made during all stages of product design and lifecycle can have implications for sterilization options

How does TIR100 help?

- TIR100 is not a radiation specific document but provides guidance on decision making at each of the stages that can affect the ability of a product to be radiation sterilized.

- Can I choose radiation compatible materials?

- Where is my sterilization capacity?

- How is my product quality maintained?

- What will my sources of bioburden be?

- What controls are in my work environment?

- Are my requirements being met?

Design for Sterilization - Examples

Materials selection and intended function

- Alternate materials, e.g. PCTFE or PVF vs PTFE or Radiation stabilized PP vs PP
- Leachables/extractables post-sterilization (plasticizers, fillers, additives, antioxidants) affecting biocompatibility
- Potential for beneficial sterilization induced changes (i.e. annealing, reducing solvents, curing hydrophilic coatings)
- Residuals as a function of mode of patient contact and patient population
- Does the product need to be sterile? (accessories, cables)

Design and Manufacturing

- Tight interferences between mated surfaces (e.g. stoppers, metal-metal, etc.)
- Areas of high density
- Bioburden controls requirements for manufacturing environment and incoming materials

Testing protocols

- Extent of verification testing allows re-sterilization and/or response to deviations in process

Packaging Considerations

- Gas permeability may impact shelf life for combination products that have oxygen sensitivity – added packaging step vs qualifying radiation process
- Orientation of product within packaging, repeatability and rigidity for radiation processes
- Amount of material going through sterilizer and impact on process efficiency and fugitive emissions
- Size of product box relative to sterilizer

Sterilization Site

- Capacity availability and back up
- Turn around time and inventory considerations
- Carbon footprint and/or extra packaging associated with transportation
- Cold chain or special environmental requirements

Regulatory efficiencies

- Time to market – novel vs established, predicate products etc.
- Product families – leveraging existing product testing data

TIR17 – Compatibility of materials

- TIR17 is a resource that can be used in new product design when selecting materials for a health care product
- Valuable update provided in 2017, but as materials evolve and new sterilization methods develop, new information should be incorporated
- Work on the next revision is underway
  - Better guidance on ranking systems for material compatibility
  - Modality selection process guidance
  - Guidance on appropriate challenge conditions and testing
  - Guidance on evaluating changing modalities?

TIR104 – Transfer between radiation sources

- TIR104 was initiate to clarify (and correct) information in ISO 11137-1 on transfer between radiation sources
- Evaluation of process capability when making the decision to transfer
  - Can the irradiator physically deliver the dose required?
  - Will dose specifications need to be updated (and what is the likelihood of success?)
- Guidance on transfer of both:
  - Sterilization dose
  - Maximum acceptable dose

Transfer fundamentals

Minimum Dose is Dose

- When product is dry, sterilization and verification doses do NOT need to be re-established
- When product is wet or can support microbial growth, a dose audit can be used to verify that sterilization dose is appropriate
  - Also applies to changing locations with same modality

Maximum Dose is not always Dose

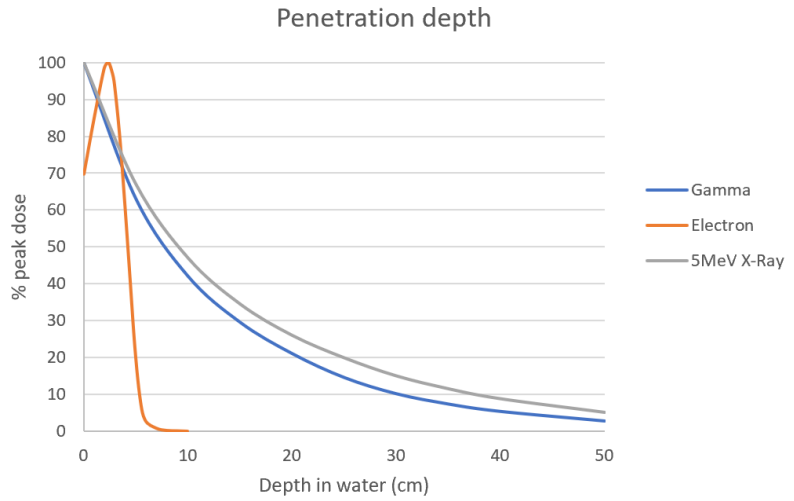
- Dose rate and temperature may have an impact on maximum dose suitability
- In general transfers from low dose rate to high will not require retesting unless a new maximum dose needs to be established to meet DUR requirements
- Activation assessment required for e-beam >10MeV or x-ray >5MeV

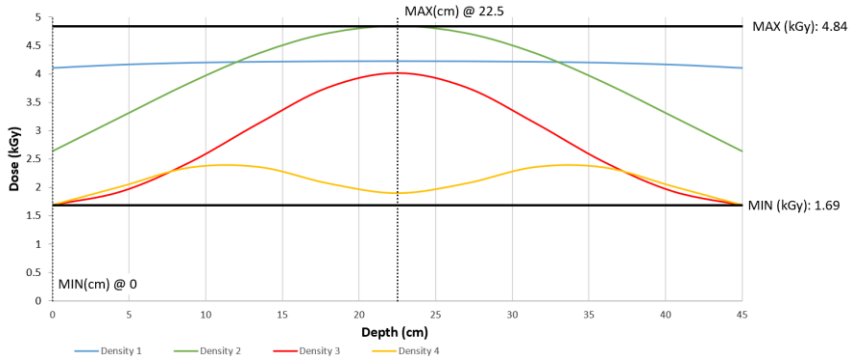
TIR104 – End-to-end considerations

- How easy it is to transfer dose depends on how much information you already know about your product
  - Sterilization dose: How did you determine? What bioburden controls do you have in place to reduce minimum dose?
  - Maximum acceptable dose: Do you know your REAL maximum dose or did you just challenge the process you had available?
- Does your product rely on the sterilization process for a functionality enhancement vs failure?
  - Crosslinking that makes product or packaging stronger?
  - Heating which anneals or cures

Transfer – How design elements help

- Packaging: Does your packaging design allow for a presentation to both electrons and photons?
  - Try not to have high density areas overlap
  - Try to keep nuclear thickness as uniform as possible
  - Consider both single unit and shipper configurations
  - Will your package size work at multiple irradiators (i.e. pallet vs tote vs conveyor)
- Is your packaging and product together designed to allow for heat transfer out of the package?
- Can your product be flipped for a vertical electron beam process?





Other work in standards

ISO 11137-1 revision

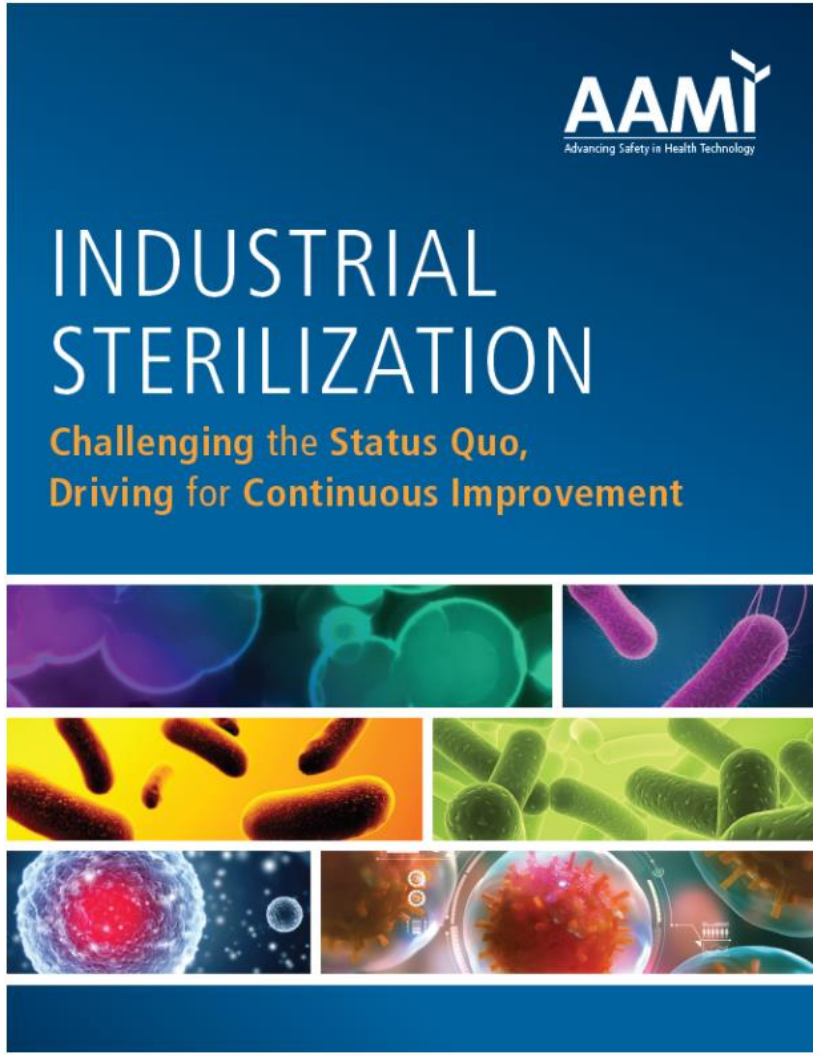
- Align with ASTM standards and ISO 11137-3 and -4
- Align with ISO 11137-2 and 13004
- Provide more specific allowances and guidance for parametric release
- Look at changing the threshold for activation assessment
- Align with TIR104

ASTM new documents

- Provide better technology specific OQ guidance
  - Gamma completed
  - Electron beam in process
  - X-ray next!
- Update and author standards as appropriate to be referenced in revised ISO 11137-1

Other publications

- Peer reviewed publications can lay the groundwork for future guidance and standards
- Two recent groups of AAMI BI&T supplements organized by the Kilmer Collaboration team, article are referenced in TIR104:
  - Industrial Sterilization, Process Optimization and Modality Changes: www.aami.org/sterilization-supplement-2020
  - Industrial Sterilization, Challenging the Status Quo, Driving for Continuous Improvement: https://www.aami.org/news-resources/publications/bi-t/is-supplement/is-supplement-2021
- Articles published in Radiation Physics & Chemistry on specific topics also used to support TIR17, ISO11137-1 including outputs from Team Nablo and IMRP



In summary

- New guidance will help ***accelerate*** the adoption of machine source radiation sterilization technology
- Consideration of **end-to-end** product lifecycle will make modality transitions easier
- **Coordination** between different standards organizations is key
- Standards work is a great example of **collaboration** to meet the needs of the health care product sterilization community
  - There are opportunities to ***get involved***, please take advantage!